

# HYPOTHESIS PROPOSAL FORM

## Part I: Guide for Writing Your Core Hypothesis Proposal

### Definition of Information Needed in Working Group Description of Hypothesis

A National Children's Study hypothesis is a scientifically compelling hypothesis of public health importance that is feasible to test and that clearly shows the need for a longitudinal family cohort study of this size and prospective nature. The hypotheses will determine the overall Study design, sample size, and the Study duration. The level of specificity about exposures, outcomes, and anticipated measures to be provided on the hypothesis should be sufficient to clearly assist National Children's Study protocol development *and* show the need for a longitudinal study of ~100,000 subjects. Many other valuable hypotheses, not fulfilling all the above criteria, will be included in the final design of the Study and should also use the format proposed below, as well as information requested by the National Children's Study Advisory Committee (NCSAC).

### General Points to Consider When Developing and Revising Your Hypothesis

- The word exposures is used repeatedly below. It is used broadly to include social, chemical, physical, biological, and nutritional factors. For example, a child may be exposed to a neighborhood with no playgrounds, to a specific industrial chemical, to a specific virus *in utero*, to a school with low per capita funding, to diets low in vegetables and fruits, etc.
- What is/are the overarching question(s)?
  - For each, what are the specific aims/hypotheses?
  - Are any of these hypotheses absolutely essential to study in this *longitudinal* cohort study (i.e., are not and would not be studied elsewhere)? For each hypothesis, indicate if the reason the hypothesis is absolutely essential is due to:
    - a) Time sequencing of exposures and outcomes with respect to development (prior to conception, during pregnancy, during infancy, childhood, adolescence, etc.)
      - i) Measurement of exposures during development (which *specific* exposures are of highest priority, when should they be measured, where should they be measured, how should they be measured)
      - ii) Measurement of outcomes during development (which *specific* outcomes will be measured, when should they be measured, how should they be measured, will measurement of the outcome change with age, etc.)
    - b) Inability to obtain the measurement in a retrospective manner
    - c) The need for repeated measures (e.g., change in exposure, cumulative exposure)

- Do any of these hypotheses require a sample size of 100,000, based on one or any of the criteria below? (Be as specific as possible: include power calculations if at all possible.) The majority of the draft hypotheses have information about prevalence of the outcome as an indicator of statistical needs and feasibility. However, the revision needs to consider statistical issues when the “sub-hypotheses” are tested and the specific groups being exposed to a particular scenario are smaller.
- For each hypothesis, indicate if the reason the hypothesis requires this sample size is due to:
  - a) Need to study sub-group exposures, susceptible sub-groups (e.g., for a specific exposure of interest, what is the likely occurrence and distribution of exposure across the one subpopulation of interest)
  - b) Need to study multiple overlapping exposures (e.g., lead, social class, family structure, neighborhood characteristics, etc.)
  - c) Need to study interactions
  - d) Rarity of outcome or exposure
  - e) Low relative risk
- Is there one, single “burning” hypothesis (either rare exposure/outcome or low relative risk) that would require investigation of the entire cohort?
- Is the hypothesis and the feasibility of testing it in the Study described with enough specificity that it may be screened and meaningfully evaluated by the Study Design WG and the NCSAC for the following components? Please note that the exposure and outcome can be positive or negative (act to enhance development or impair development, produce disease or health).
  - a) Specific exposures of interest
  - b) Developmental periods during which those exposures can act and should be measured
  - c) Description of where and how the exposure should be measured
  - d) Specific description of the outcomes likely to be modified by the identified exposures
  - e) When the outcomes should be assessed across development
  - f) How the outcomes should be evaluated

## **Part II: Hypothesis Submission Form**

Please limit your response to 4–7 pages

### **I. Proposed Hypothesis**

Include what is the highest priority exposures and primary outcome associated with this hypothesis.

Exposures:

- What are the specific exposures of interest, in what priority?
- When should the exposures be measured?
- How should the exposures be measured?

Outcomes:

- When should the outcomes be measured?
- What tools should be used for measuring the outcome?

### **II. Lead Working Group and Contact Person (include phone and e-mail)**

### **III. Working Groups on Team and Contact Person for Each of Those Groups**

### **IV. Public Health Significance**

Please address the following issues to the extent possible for both the exposure and outcome:

- Prevalence/incidence
- Morbidity
- Quality of life
- Mortality
- Economic burden to individual, family, community, etc.
- Social burden to individual, family, etc.
- Perceived importance: how is answering this hypothesis going to improve the health and development of children?
- Preventability/Malleability

### **V. Need for a Large, Prospective, Longitudinal Study**

- Time sequencing
- Need for repeated measures (e.g., change in exposure, cumulative exposure, etc.)
- Need for a sample size of approximately 100,000 based on one or any of the criteria below. (Be as specific as possible: include power calculation if at all possible.)
  - Need to study sub-group exposures, susceptible sub-groups
  - Need to study multiple overlapping exposures
  - Need to study interactions
  - Does this hypotheses have such a rare exposure/outcome or low relative risk that it would require investigation using the entire cohort of 100,000?

## **VI. Scientific Merit**

Please address the following issues to the extent possible:

- What theory supports the hypothesis?
- Current scientific understanding
  - Non-human experimental data supporting the hypothesis
  - Non-human experimental data supporting the hypothesis at exposure levels experienced by humans
  - Human data supporting the hypothesis
- How will answering this hypothesis/question advance our understanding?

## **VII. Potential for Innovative Research**

- New findings
- New technologies

## **VIII. Feasibility**

Please address the following issues to the extent possible:

- Critical period for exposure and outcomes
- Sampling needs: targeted groups or settings, special strategies, sample size (provide power calculations if possible), special sub-groups of interest, etc.
- Contact: if more than one contact is needed, frequency and timing of the recontact
- Measurement tools for assessing exposures or outcomes: questionnaires, educational or psychological testing, medical diagnosis or clinical assessments, biological specimens, interviews
- For each measurement tool:
  - Have the measurement tools been demonstrated to be valid and reliable in the population in which the Study will use them?
  - Is specialized expertise and equipment needed?
  - Is there sufficient capacity to measure these factors on a large scale?
  - What are the estimated costs of the measurements?
  - What are the risks associated with these measurements?
  - Are there other ethical considerations associated with these measurements (e.g., reporting issues, etc.)?
  - What are the burden to the participant and family associated with these measurements?
- Community Involvement
- Other burden to the participant and family associated with this hypothesis not covered in the measurement tool section